

2/9/160 (Item 63 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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DIALOG  
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08103291 BIOSIS NO.: 000042095489  
DIPHTHERIA TOXIN B FRAGMENT MUTANTS CYTOTOXICITY ON VERO CELLS  
AND PORE

FORMATION ACTIVITY

AUTHOR: CABIAUX V; MINDELL J; COLLIER R J

AUTHOR ADDRESS: DEP. MICROBIOL. MOL. GENET., HARVARD MED. SCH., 200  
LONGWOOD AVE., BOSTON, MASS. 02115.

JOURNAL: JOINT ANNUAL MEETING OF THE BIOPHYSICAL SOCIETY AND THE  
AMERICAN

SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY, HOUSTON, TEXAS,  
USA,

FEBRUARY 9-13, 1992. BIOPHYS J 61 (2 PART 2). 1992. A211. 1992

CODEN: BIOJA

DOCUMENT TYPE: Meeting

RECORD TYPE: Citation

LANGUAGE: ENGLISH

DESCRIPTORS: ABSTRACT

CONCEPT CODES:

02506 Cytology and Cytochemistry-Animal

10064 Biochemical Studies-Proteins, Peptides and Amino Acids

22501 Toxicology-General; Methods and Experimental

36002 Medical and Clinical Microbiology-Bacteriology

00520 General Biology-Symposia, Transactions and Proceedings of  
Conferences, Congresses, Review Annuals

32500 Tissue Culture, Apparatus, Methods and Media

BIOSYSTEMATIC CODES:

08890 Irregular Nonsporing Gram-Positive Rods (1992- )

86190 Primates-Unspecified

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA):

Microorganisms

Bacteria

Eubacteria

Animals

Chordates

Vertebrates

Nonhuman Vertebrates

Mammals

Nonhuman Mammals

Primates

Nonhuman Primates

SYSTEM:OS - DIALOG OneSearch

File 155: MEDLINE(R) 1966-2002/Sep W5

\*File 155: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 5:Biosis Previews(R) 1969-2002/Sep W5  
(c) 2002 BIOSIS

\*File 5: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 73:EMBASE 1974-2002/Sep W5  
(c) 2002 Elsevier Science B.V.

\*File 73: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 143:Biol. & Agric. Index 1983-2002/Aug  
(c) 2002 The HW Wilson Co

File 65:Inside Conferences 1993-2002/Sep W5  
(c) 2002 BLDSC all rts. reserv.

File 10:AGRICOLA 70-2002/Sep  
(c) format only 2002 The Dialog Corporation

File 94:JICST-EPlus 1985-2002/Jul W4  
(c) 2002 Japan Science and Tech Corp(JST)

\*File 94: There is no data missing. UDs have been adjusted to reflect the current months data. See Help News94 for details.

File 35:Dissertation Abs Online 1861-2002/Sep  
(c) 2002 ProQuest Info&Learning

File 342:Derwent Patents Citation Indx 1978-01/200224  
(c) 2002 Thomson Derwent

\*File 342: Updates 200160-200209 replaced. See HELP NEWS 342.

Alert feature enhanced for multiple files, etc. See HELP ALERT.

File 357:Derwent Biotech Res. 1982-2002/June W1  
(c) 2002 Thomson Derwent & ISI

\*File 357: File enhancements now online. See HELP NEWS 357.

Alert feature enhanced for multiple files, etc. See HELP ALERT.

File 340:CLAIMS(R)/US Patent 1950-02/Oct 01  
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\*File 340: Application & grant publications are in 1 record. See HELP NEWS340 & HELP ALERTS340 for search, display & Alert info.

Set	Items	Description
Executing	TD608	
>>>SET HIGHLIGHT: use ON, OFF, or 1-5 characters		
>>>File 155 processing for FORM? stopped at FORMYLOXYMETHYLURIDINE		
>>>File 5 processing for FORM? stopped at FORMYLISOCOUMARIN		
>>>File 73 processing for FORM? stopped at FORMYLPIPERIDINE		
>>>File 340 processing for FORM? stopped at FORMULULA		
Processing		
Processed	10 of 11 files ...	
Completed	processing all files	
	28114 PORE?/TI	
	1308435 FORM?/TI	
	100239 TOXIN?/TI	
S1	419 PORE?/TI AND FORM?/TI AND TOXIN?/TI	
?rd		
>>>Duplicate detection is not supported for File 342.		
>>>Duplicate detection is not supported for File 340.		

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>>>Records from unsupported files will be retained in the RD set.

...examined 50 records (50)

...examined 50 records (100)

...examined 50 records (150)

...examined 50 records (200)

...examined 50 records (250)

...examined 50 records (300)

...examined 50 records (350)

...examined 50 records (400)

...completed examining records

S2 212 RD (unique items)

?t s2/3,kwic/210

4th International Workshop on Pore - Forming Toxins . 14-17 September 2000, Trento, Italy. Abstracts.

Medical microbiology and immunology (Germany) Sep 2000, 189 (1) p27-54, ISSN 0300-8584 Journal Code: 0314524

Document type: Congresses; Overall

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Tags: Animal; Human

Descriptors: \*Toxins; Cell Membrane; Toxins--pharmacology--PD

CAS Registry No.: 0 (Toxins)

Record Date Created: 20010125

2/9/16 (Item 16 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

11322907 21371764 PMID: 11478872

Beta-barrel pore - forming toxins : intriguing dimorphic proteins.

Heuck A P; Tweten R K; Johnson A E

Department of Medical Biochemistry and Genetics, Texas A&M University System Health Science Center, College Station, Texas 77843-1114, USA.

Biochemistry (United States) Aug 7 2001, 40 (31) p9065-73, ISSN 0006-2960 Journal Code: 0370623

Contract/Grant No.: AI 37657; AI; NIAID

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

(64 Refs.)

Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: \*Bacterial Toxins--chemistry--CH; \*Membrane Proteins --chemistry--CH; Amino Acid Motifs; Amino Acid Sequence; Bacterial Toxins --classification--CL; Bacterial Toxins--metabolism--ME; Cell Membrane --chemistry--CH; Cell Membrane--metabolism--ME; Cell Membrane --microbiology--MI; Membrane Proteins--classification--CL; Membrane Proteins--metabolism--ME; Molecular Sequence Data; Protein Folding; Protein Structure, Secondary

CAS Registry No.: 0 (Bacterial Toxins); 0 (Membrane Proteins)

Record Date Created: 20010731

2/9/17 (Item 17 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

11317981 21364107 PMID: 11470547

Molecular characterization of the pore - forming toxin , pyolysin, a major virulence determinant of *Arcanobacterium pyogenes*.

Billington S J; Songer J G; Jost B H

Department of Veterinary Science and Microbiology, The University of Arizona, 1117 East Lowell Street, Tucson, AZ 85721, USA.  
sbilling@u.arizona.edu

Veterinary microbiology (Netherlands) Sep 28 2001, 82 (3) p261-74,  
ISSN 0378-1135 Journal Code: 7705469

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

*Arcanobacterium pyogenes* is a common inhabitant and opportunistic pathogen of domestic animals. The pathogenesis of this organism in a range of suppurative diseases is not well understood. However, the development of genetic techniques to study this organism has allowed advances in the analysis of *A. pyogenes* virulence factors. A major step in this analysis was the identification and cloning of the *A. pyogenes* hemolytic exotoxin, pyolysin (PLO). PLO is the most divergent member of the cholesterol-binding pore-forming family of toxins. PLO is also divergent in a C-terminal undecapeptide motif which is almost invariant among other members of the family. This divergent undecapeptide motif is required for the full cytolytic activity of PLO and is also responsible for its oxygen-resistant nature. Insertional inactivation of the plo gene results in a significant reduction in virulence in an intraperitoneal mouse model of infection. The virulence of the plo mutant can be restored by providing PLO in trans, suggesting that PLO is a major virulence factor in *A. pyogenes* pathogenesis in mice. Results of previous vaccination trials with crude antigens against *A. pyogenes* infection in domestic animals and mice have been equivocal at best. However, a recombinant PLO-based subunit vaccine protected mice from experimental *A. pyogenes* infection, indicating that PLO is also an important host protective antigen. These results provide promise that the dogma that domestic animals are recalcitrant to vaccination against *A. pyogenes* infection may prove false.

Tags: Animal; Support, U.S. Gov't, Non-P.H.S.

Descriptors: \*Actinomycetaceae--pathogenicity--PY; \*Actinomycetales Infections--veterinary--VE; \*Hemolysins--genetics--GE; --Actinomyces--genetics--GE; Actinomyces--immunology--IM; Actinomyces--pathogenicity--PY; Actinomycetaceae--genetics--GE; Actinomycetaceae--immunology--IM; Actinomycetales Infections--microbiology--MI; Antigens, Bacterial --physiology--PH; Cytotoxicity Tests, Immunologic; Disease Models, Animal;

---

Hemolysins--physiology--PH; Mice; Mutagenesis; Vaccination--veterinary--VE;  
Virulence  
CAS Registry No.: 0 (Antigens, Bacterial); 0 (Hemolysins); 0  
(pyolysin)  
Record Date Created: 20010725

2/9/19 (Item 19 from file: 155)  
DIALOG(R)File 155: MEDLINE(R)

11268333 21310790 PMID: 11417117  
Pore - forming bacterial protein toxins : an overview.  
Alouf J E  
Institut Pasteur 28, rue du Dr. Roux, 75724 Paris, France.  
Current topics in microbiology and immunology (Germany) 2001, 257  
p1-14, ISSN 0070-217X Journal Code: 0110513  
Document type: Journal Article  
Languages: ENGLISH  
Main Citation Owner: NLM  
Record type: Completed  
Subfile: INDEX MEDICUS  
Descriptors: \*Bacteria--metabolism--ME; \*Bacterial Proteins  
--classification--CL; \*Cytotoxins--classification--CL; Bacteria--pathogenic  
ity--PY; Cell Membrane Permeability; Gram-Negative Bacteria--metabolism--ME  
; Gram-Positive Bacteria--metabolism--ME; Virulence  
; CAS Registry No.: 0 (Bacterial Proteins); 0 (Cytotoxins)  
Record Date Created: 20010621

2/9/25 (Item 25 from file: 155)  
DIALOG(R)File 155: MEDLINE(R)

11010368 20562499 PMID: 11111916  
Structural basis of pore formation by cholesterol-binding toxins .  
Gilbert R J; Jimenez J L; Chen S; Andrew P W; Saibil H R  
Division of Structural Biology, Wellcome Trust Centre for Human Genetics,  
Oxford, UK. [gilbert@strbi.ox.ac.uk](mailto:gilbert@strbi.ox.ac.uk)  
International journal of medical microbiology : IJMM (GERMANY) Oct 2000  
, 290 (4-5) p389-94, ISSN 1438-4221 Journal Code: 100898849  
Document type: Journal Article  
Languages: ENGLISH  
Main Citation Owner: NLM  
Record type: Completed  
Subfile: INDEX MEDICUS  
In this paper we describe reconstructions by electron cryo-microscopy of

two oligomeric states of the pore-forming toxin pneumolysin. The results are interpreted by the fitting of atomic models of separated domains to the 3-dimensional electron density maps, revealing two steps in the mechanism of pore formation by the family of cholesterol-binding toxins. We briefly describe the observation of the toxin pore in model membranes and contrast the apparent mechanism of pneumolysin with that of other pore-forming toxins.

Descriptors: \*Cholesterol--metabolism--ME; \*Cytotoxins--chemistry--CH; \*Streptolysins--chemistry--CH; Bacterial Toxins--chemistry--CH; Microscopy, Electron; Protein Conformation; Protein Subunits

CAS Registry No.: 0 (Bacterial Toxins); 0 (Cytotoxins); 0 (Protein Subunits); 0 (Streptolysins); 0 (pneumolysin); 57-88-5 (Cholesterol); 71329-60-7 (Clostridium perfringens theta-toxin)

Record Date Created: 20010419

2/9/29 (Item 29 from file: 155)  
DIALOG(R)File 155: MEDLINE(R)

10689456 20219650 PMID: 10754575

Adventures of a pore-forming toxin at the target cell surface.

Abrami L; Fivaz M; van der Goot F G

Dept of Biochemistry, University of Geneva, 30 quai E. Ansermet, 1211 Geneva 4, Switzerland.

Trends in microbiology (ENGLAND) Apr 2000, 8 (4) p168-72, ISSN 0966-842X Journal Code: 9310916

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The past three years have shed light on how the pore-forming toxin aerolysin binds to its target cell and then hijacks cellular devices to promote its own polymerization and pore formation. This selective permeabilization of the plasma membrane has unexpected intracellular consequences that might explain the importance of aerolysin in *Aeromonas* pathogenicity. (31 Refs.)

Tags: Animal; Human

Descriptors: \*Aeromonas hydrophila--pathogenicity--PY; \*Bacterial Toxins--metabolism--ME; \*Cell Membrane--metabolism--ME; Aeromonas hydrophila--metabolism--ME; Bacterial Toxins--chemistry--CH; Bacterial Toxins--toxicity--TO; Biopolymers--metabolism--ME; Cell Membrane--drug effects--DE; Cell Membrane--microbiology--MI; Cell Membrane Permeability--drug effects--DE; Receptors, Cell Surface--chemistry--CH; Receptors, Cell Surface--metabolism--ME

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CAS Registry No.: 0 (Bacterial Toxins); 0 (Biopolymers); 0 (Receptors, Cell Surface); 53126-24-2 (aerolysin)  
Record Date Created: 20000512

2/9/31 (Item 31 from file: 155)  
DIALOG(R)File 155: MEDLINE(R)

10553669 20091013 PMID: 10623563

Clostridium perfringens beta-toxin forms multimeric transmembrane pores in human endothelial cells.

Steinthorsdottir V; Halldorsson H; Andresson O S

Institute for Experimental Pathology, University of Iceland, Reykjavik, Keldur, 112, Iceland. vstein@decode.is

Microbial pathogenesis (ENGLAND) Jan 2000, 28 (1) p45-50, ISSN 0882-4010 Journal Code: 8606191

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Beta-toxin is one of the lethal toxins of *Clostridium perfringens*. It shares sequence homology with the pore-forming alpha-toxin of *Staphylococcus aureus* and structural homology has been indicated by mutagenesis studies. Human endothelial cells are sensitive to the toxic effect of alpha-toxin and in order to investigate the function of beta-toxin we have looked at the effect of the protein on human umbilical vein endothelial cells. We show that like alpha-toxin beta-toxin induces release of arachidonic acid in a dose dependent manner. In addition we show that both toxins cause leakage of inositol from the cells, consistent with the formation of transmembrane pores. The effect of toxin mutants on endothelial cells correlates with the lethal dose of each mutant in mice. Furthermore, we demonstrate the formation of heat stable toxin multimers in the cell membrane. Multimer formation was not observed on other cell types tested. We conclude that beta-toxin is a cell specific pore-forming toxin, structurally and functionally related to alpha-toxin of *Staphylococcus aureus*. Copyright 2000 Academic Press.

Tags: Animal; Human; Support, Non-U.S. Gov't

Descriptors: \*Bacterial Toxins--chemistry--CH; \*Clostridium perfringens--pathogenicity--PY; \*Endothelium, Vascular--drug effects--DE; Arachidonic Acid--secretion--SE; Bacterial Toxins--toxicity--TO; Calcium--metabolism--ME; Cell Membrane--drug effects--DE; Cells, Cultured; Inositol Phosphates--metabolism--ME; Mice; Phospholipase C--toxicity--TO

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CAS Registry No.: 0 (Bacterial Toxins); 0 (Clostridium perfringens beta-toxin); 0 (Inositol Phosphates); 506-32-1 (Arachidonic Acid);

7440-70-2 (Calcium)  
Enzyme No.: EC 3.1.4.- (Clostridium perfringens alpha-toxin); EC  
3.1.4.3 (Phospholipase C)  
Record Date Created: 20000207

2/9/36 (Item 36 from file: 155)  
DIALOG(R)File 155: MEDLINE(R)

10473549 20021616 PMID: 10555145

The mechanism of membrane insertion for a cholesterol-dependent cytolysin: a novel paradigm for pore-forming toxins.  
Shatursky O; Heuck A P; Shepard L A; Rossjohn J; Parker M W; Johnson A E; Tweten R K

Department of Microbiology and Immunology, The University of Oklahoma Health Sciences Center, Oklahoma City 73190, USA.

Cell (UNITED STATES) Oct 29 1999, 99 (3) p293-9, ISSN 0092-8674

Journal Code: 0413066

Contract/Grant No.: AI37657; AI; NIAID

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Perfringolysin O (PFO), a water-soluble monomeric cytolysin secreted by pathogenic Clostridium perfringens, oligomerizes and forms large pores upon encountering cholesterol-containing membranes. Whereas all pore-forming bacterial toxins examined previously have been shown to penetrate the membrane using a single amphipathic beta hairpin per polypeptide, cysteine-scanning mutagenesis and multiple independent fluorescence techniques here reveal that each PFO monomer contains a second domain involved in pore formation, and that each of the two amphipathic beta hairpins completely spans the membrane. In the soluble monomer, these transmembrane segments are folded into six alpha helices. The insertion of two transmembrane hairpins per toxin monomer and the major change in secondary structure are striking and define a novel paradigm for the mechanism of membrane insertion by a cytolytic toxin.

Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Descriptors: \*Bacterial Toxins--chemistry--CH; \*Bacterial Toxins--metabolism--ME; \*Clostridium perfringens--physiology--PH; \*Liposomes; Amino Acid Sequence; Amino Acid Substitution; Bacterial Toxins--genetics--GE; Cysteine; Fluorescent Dyes; Hemolysins--metabolism--ME; Models, Biological; Models, Molecular; Molecular Sequence Data; Mutagenesis, Site-Directed; Phosphatidylcholines; Protein Structure, Secondary;

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Recombinant Proteins--chemistry--CH; Recombinant Proteins--metabolism--ME;

Spin Labels

CAS Registry No.: 0 (Bacterial Toxins); 0 (Fluorescent Dyes); 0 (Hemolysins); 0 (Liposomes); 0 (Phosphatidylcholines); 0 (Recombinant Proteins); 0 (Spin Labels); 52-90-4 (Cysteine); 6753-55-5 (1-palmitoyl-2-oleoylphosphatidylcholine); 71329-60-7 (Clostridium perfringens theta-toxin)

Record Date Created: 19991123

2/9/39 (Item 39 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

10364251 99359379 PMID: 10429196

Cysteine-scanning mutagenesis of an eukaryotic pore-forming toxin from sea anemone: topology in lipid membranes.

Anderluh G; Barlic A; Podlesek Z; Macek P; Pungercar J; Gubensek F; Zecchini M L; Serra M D; Menestrina G

Department of Biology, Biotechnical Faculty, University of Ljubljana, Slovenia. gregor.anderluh@uni-lj.si

European journal of biochemistry / FEBS (GERMANY) Jul 1999, 263 (1) p128-36, ISSN 0014-2956 Journal Code: 0107600

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Equinatoxin II is a cysteineless pore-forming protein from the sea anemone *Actinia equina*. It readily creates pores in membranes containing sphingomyelin. Its topology when bound in lipid membranes has been studied using cysteine-scanning mutagenesis. At approximately every tenth residue, a cysteine was introduced. Nineteen single cysteine mutants were produced in *Escherichia coli* and purified. The accessibility of the thiol groups in lipid-embedded cysteine mutants was studied by reaction with biotin maleimide. Most of the mutants were modified, except those with cysteines at positions 105 and 114. Mutants R144C and S160C were modified only at high concentrations of the probe. Similar results were obtained if membrane-bound biotinylated mutants were tested for avidin binding, but in this case three more mutants gave a negative result: S1C, S13C and K43C. Furthermore, mutants S1C, S13C, K20C, K43C and S95C reacted with biotin only after insertion into the lipid, suggesting that they were involved in major conformational changes occurring upon membrane binding. These results were further confirmed by labeling the mutants with acrylodan, a polarity-sensitive fluorescent probe. When labeled mutants were combined with vesicles, the following mutants exhibited blue-shifts, indicating the

transfer of acrylodan into a hydrophobic environment: S13C, K20C, S105C, S114C, R120C, R144C and S160C. The overall results suggest that at least two regions are embedded within the lipid membrane: the N-terminal 13-20 region, probably forming an amphiphilic helix, and the tryptophan-rich 105-120 region. Arg144, Ser160 and residues nearby could be involved in making contacts with lipid headgroups. The association with the membrane appears to be unique and different from that of bacterial pore-forming proteins and therefore equinatoxin II may serve as a model for eukaryotic channel-forming toxins.

Tags: Animal; Support, Non-U.S. Gov't

Descriptors: \*Cnidarian Venoms--chemistry--CH; \*Cnidarian Venoms--genetics--GE; \*Sea Anemones--chemistry--CH; \*Sea Anemones--genetics--GE; 2-Naphthylamine--analogs and derivatives--AA; Amino Acid Sequence; Amino Acid Substitution; Avidin; Binding Sites--genetics--GE; Biotin; Cloning, Molecular; Cysteine--chemistry--CH; Liposomes; Membrane Lipids--chemistry--CH; Models, Molecular; Molecular Probes; Molecular Sequence Data; Mutagenesis, Site-Directed; Protein Conformation; Solutions

CAS Registry No.: 0 (Cnidarian Venoms); 0 (Liposomes); 0 (Membrane Lipids); 0 (Molecular Probes); 0 (Solutions); 1405-69-2 (Avidin); 52-90-4 (Cysteine); 54578-46-0 (equinatoxin); 58-85-5 (Biotin); 86636-92-2 (acrylodan); 91-59-8 (2-Naphthylamine)

Record Date Created: 19990817

2/9/58 (Item 58 from file: 155)  
DIALOG(R)File 155: MEDLINE(R)

09005293 96353913 PMID: 8755571

Pore - forming toxins trigger shedding of receptors for interleukin 6 and lipopolysaccharide.

Walev I; Vollmer P; Palmer M; Bhakdi S; Rose-John S

Institute of Medical Microbiology and Hygiene, Johannes Gutenberg

University of Mainz, Germany.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Jul 23 1996, 93 (15) p7882-7, ISSN 0027-8424

Journal Code: 7505876

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Cleavage of membrane-associated proteins with the release of biologically active macromolecules is an emerging theme in biology. However, little is known about the nature and regulation of the involved proteases or about the physiological inducers of the shedding process. We here report that

rapid and massive shedding of the interleukin 6 receptor (IL-6R) and the lipopolysaccharide receptor (CD14) occurs from primary and transfected cells attacked by two prototypes of pore-forming bacterial toxins, streptolysin O and Escherichia coli hemolysin. Shedding is not induced by an streptolysin O toxin mutant which retains cell binding capacity but lacks pore-forming activity. The toxin-dependent cleavage site of the IL-6R was mapped to a position close to, but distinct from, that observed after stimulation with phorbol myristate acetate. Soluble IL-6R that was shed from toxin-treated cells bound its ligand and induced an IL-6-specific signal in cells that primarily lacked the IL-6R. Transsignaling by soluble IL-6R and soluble CD14 is known to dramatically broaden the spectrum of host cells for IL-6 and lipopolysaccharide, and is thus an important mechanism underlying their systemic inflammatory effects. Our findings uncover a novel mechanism that can help to explain the long-range detrimental action of pore-forming toxins in the host organism.

Tags: Animal; Human; Support, Non-U.S. Gov't

Descriptors: \*Antigens, CD--drug effects--DE; \*Antigens, CD14 --drug effects--DE; \*Hemolysins--pharmacology--PD; \*Macrophages--immunology--IM; \*Monocytes--immunology--IM; \*Receptors, Interleukin--drug effects--DE; \*Streptolysins--pharmacology--PD; Antigens, CD--biosynthesis--BI; Antigens, CD14--biosynthesis--BI; Cell Line; Cells, Cultured; Cercopithecus aethiops; Enzyme Inhibitors--pharmacology--PD; Enzyme-Linked Immunosorbent Assay; Escherichia coli; Haptoglobins--biosynthesis--BI; Kinetics; Macrophages --drug effects--DE; Monocytes--drug effects--DE; Receptors, Interleukin --biosynthesis--BI; Receptors, Interleukin-6; Recombinant Proteins --biosynthesis--BI; Recombinant Proteins--drug effects--DE; Signal Transduction; Staurosporine--pharmacology--PD; Tetradeconoylphorbol Acetate --pharmacology--PD; Transfection; Tumor Cells, Cultured  
CAS Registry No.: 0 (Antigens, CD); 0 (Antigens, CD14); 0 (Enzyme Inhibitors); 0 (Haptoglobins); 0 (Hemolysins); 0 (Receptors, Interleukin); 0 (Receptors, Interleukin-6); 0 (Recombinant Proteins); 0 (Streptolysins); 0 (streptolysin O); 16561-29-8 (Tetradeconoylphorbol Acetate); 62996-74-1 (Staurosporine)

Record Date Created: 19961029

2/9/73 (Item 73 from file: 155)  
DIALOG(R)File 155: MEDLINE(R)

08088000 94212360 PMID: 8160187

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Pore - formation by Escherichia coli hemolysin (HlyA) and other members of the RTX toxins family.

Menestrina G; Moser C; Pellet S; Welch R

CNR Centro di Fisica degli Stati Aggregati, Povo, Trento, Italy.

Toxicology (IRELAND) Feb 28 1994, 87 (1-3) p249-67, ISSN 0300-483X

Journal Code: 0361055

Contract/Grant No.: AI 20323; AI; NIAID

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Escherichia coli hemolysin (HlyA) is a major cause of *E. coli* virulence. It lyses erythrocytes by a colloid osmotic shock due to the formation of hydrophilic pores in the cell wall. The size of these channels can be estimated using osmotic protectant of increasing dimensions. To show that the formation of pores does not depend critically on the osmotic swelling we prepared resealed human erythrocyte ghosts loaded with a fluorescent marker. When attacked by HlyA the internal marker was released, indicating the formation of toxin channels so large as to let it through. The channels can be directly demonstrated also in purely lipidic model systems such as planar membranes and unilamellar vesicles, which lack any putative protein receptor. HlyA has been recognised as a member of a large family of exotoxins elaborated by Gram-negative organisms including *Proteus*, *Bordetella*, *Morganella*, *Pasteurella* and *Actinobacillus*. These toxins have quite different target cell specificity and in many cases are leukocidal. When tried on planar membranes however, even specific leukotoxins open channels not dissimilar from those formed by HlyA, suggesting this might be a common step in their action. Comparison of the hydrophobic properties of six members of the toxin family indicates the presence of a conserved cluster of ten contiguous amphipathic helices, located in the N-terminal half of the molecule, which might be involved in channel formation. (82

Refs.)

Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: \*Bacterial Proteins--toxicity--TO; \*Bacterial Toxins--toxicity--TO; \*Escherichia coli--pathogenicity--PY; \*Hemolysins--toxicity--TO; Bacterial Proteins--chemistry--CH; Bacterial Toxins--chemistry--CH; Cell Membrane Permeability; Erythrocytes--physiology--PH; Hemolysins--chemistry--CH; Lipid Bilayers--metabolism--ME; Membrane Potentials

CAS Registry No.: 0 (Bacterial Proteins); 0 (Bacterial Toxins); 0

(Hemolysins); 0 (HlyA protein); 0 (Lipid Bilayers)

Record Date Created: 19940519

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2/9/76 (Item 76 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

07912207 94049428 PMID: 8232070

2nd International Workshop on Pore - Forming Toxins . September  
29-October 2, 1993, Mainz, Germany. Abstracts.

Medical microbiology and immunology (GERMANY) Sep 1993, 182 (4)  
p177-221, ISSN 0300-8584 Journal Code: 0314524  
Document type: Congresses; Overall  
Languages: ENGLISH  
Main Citation Owner: NLM  
Record type: Completed  
Subfile: INDEX MEDICUS  
Tags: Animal; Human  
Descriptors: \*Bacterial Toxins--metabolism--ME; Bacterial Toxins  
--pharmacology--PD; Cell Membrane--drug effects--DE  
CAS Registry No.: 0 (Bacterial Toxins)  
Record Date Created: 19931210

2/9/84 (Item 84 from file: 155)  
DIALOG(R)File 155: MEDLINE(R)

07515103 93040368 PMID: 1358137  
1st International Workshop on Pore - Forming Toxins and their Role in  
the Competition among Different Organisms. Trento, Italy, 26-29 September  
1991.  
FEMS microbiology immunology (NETHERLANDS) Sep 1992, 5 (1-3) p1-160,  
ISSN 0920-8534 Journal Code: 8901230  
Document type: Congresses; Overall  
Languages: ENGLISH  
Main Citation Owner: NLM  
Record type: Completed  
Subfile: INDEX MEDICUS  
Tags: Animal; Human; Support, Non-U.S. Gov't  
Descriptors: \*Cell Membrane--drug effects--DE; \*Toxins--pharmacology--PD  
CAS Registry No.: 0 (Toxins)  
Record Date Created: 19921208

2/9/96 (Item 96 from file: 155)  
DIALOG(R)File 155: MEDLINE(R)

04296294 83287779 PMID: 6309569  
Localization in diphtheria toxin fragment B of a region that induces  
pore formation in planar lipid bilayers at low pH.  
Deleers M; Beugnier N; Falmagne P; Cabiaux V; Ruysschaert JM  
FEBS letters (NETHERLANDS) Aug 22 1983, 160 (1-2) p82-6, ISSN  
0014-5793 Journal Code: 0155157  
Document type: Journal Article  
Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Like diphtheria toxin and the N-terminal (Mr 23 000) region of fragment B, CB1 (Mr 13 000), the cyanogen bromide peptide located in the middle region of fragment B is able to induce pore formation in lipid bilayer membrane at low pH. These two peptides (Mr 23 000 and 13 000) share a common segment (Mr 6300) containing the predicted amphipathic, alpha-helical, transverse lipid-associating domain (Mr 2750) of fragment B [J. Cell Biol. (1980) 87, 837-840]. Therefore, we postulated this domain to be responsible for the pore formation ability of diphtheria toxin [Proc. Natl. Acad. Sci. USA (1981) 78, 172-176]. A relationship between the pH dependency of pore formation and the presence of a cluster of prolines in the C-terminal region of CB1 is proposed.

Descriptors: \*Diphtheria Toxin; \*Lipid Bilayers; Electric Conductivity; Ion Channels--metabolism--ME; Kinetics; Membrane Potentials; Models, Biological; Peptide Fragments

CAS Registry No.: 0 (Diphtheria Toxin); 0 (Ion Channels); 0 (Lipid Bilayers); 0 (Peptide Fragments); 0 (diphtheria toxin fragment A); 0 (diphtheria toxin fragment B)

Record Date Created: 19831021

2/9/98 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

(c) 2002 BIOSIS. All rts. reserv.

13779027 BIOSIS NO.: 200200407848

Mutagenesis of alpha4-alpha5 loop residues in the pore - forming domain of the bacillus thuringiensis Cry4B toxin .

AUTHOR: Kanintronkul Yodsoi(a); Panyim Sakol(a); Angsuthanasombat Chanan(a)

AUTHOR ADDRESS: (a)Int. of Molecular Biology and Genetics, Buthamonthon 4, Nakornprathom, 73170\*\*Thailand

JOURNAL: Biophysical Journal 82 (1 Part 2):p559a January, 2002

MEDIUM: print

CONFERENCE/MEETING: 46th Annual Meeting of the Biophysical Society San Francisco, California, USA February 23-27, 2002

ISSN: 0006-3495

RECORD TYPE: Citation

LANGUAGE: English

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Toxicology

BIOSYSTEMATIC NAMES: Endospore-forming Gram-Positives--Eubacteria,

Bacteria, Microorganisms; Enterobacteriaceae--Facultatively Anaerobic

Gram-Negative Rods, Eubacteria, Bacteria, Microorganisms

ORGANISMS: *Bacillus thuringiensis* (Endospore-forming Gram-Positives); *E. coli* {*Escherichia coli*} (Enterobacteriaceae)  
ORGANISMS: PARTS ETC: membrane  
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Bacteria; Eubacteria; Microorganisms  
CHEMICALS & BIOCHEMICALS: Cry4B--larvicide, structure-activity relationships, toxin  
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Poster  
CONCEPT CODES:  
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals  
10060 Biochemical Studies-General  
22501 Toxicology-General; Methods and Experimental  
31000 Physiology and Biochemistry of Bacteria  
54600 Pest Control, General; Pesticides; Herbicides  
BIOSYSTEMATIC CODES:  
06702 Enterobacteriaceae (1992- )  
07810 Endospore-forming Gram-Positives (1992- )

2/9/99 (Item 2 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2002 BIOSIS. All rts. reserv.

13778885 BIOSIS NO.: 200200407706  
Topography of the C-terminal domain of the pore - forming toxin , perfringolysin O, on the membrane surface.  
AUTHOR: Ramachandran Rajesh(a); Heuck Alejandro P(a); Tweten Rodney K; Johnson Arthur E(a)  
AUTHOR ADDRESS: (a)Texas A and M University Health Science Center, Mail Stop 1114, College Station, TX, 77843\*\*USA  
JOURNAL: Biophysical Journal 82 (1 Part 2):p530a January, 2002  
MEDIUM: print  
CONFERENCE/MEETING: 46th Annual Meeting of the Biophysical Society San Francisco, California, USA February 23-27, 2002  
ISSN: 0006-3495  
RECORD TYPE: Citation  
LANGUAGE: English  
DESCRIPTORS:  
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Membranes (Cell Biology); Toxicology

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BIOSYSTEMATIC NAMES: Endospore-forming Gram-Positives--Eubacteria, Bacteria, Microorganisms  
ORGANISMS: *Clostridium perfringens* (Endospore-forming Gram-Positives)  
ORGANISMS: PARTS ETC: membrane

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Bacteria; Eubacteria;  
Microorganisms  
CHEMICALS & BIOCHEMICALS: perfringolysin O--pore-forming toxin, toxin  
MISCELLANEOUS TERMS: protein-membrane interaction; Meeting Abstract;  
Meeting Poster

CONCEPT CODES:

- 00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
- 10060 Biochemical Studies-General
- 10508 Biophysics-Membrane Phenomena
- 22501 Toxicology-General; Methods and Experimental
- 30500 Morphology and Cytology of Bacteria
- 31000 Physiology and Biochemistry of Bacteria

BIOSYSTEMATIC CODES:

- 07810 Endospore-forming Gram-Positives (1992- )

2/9/103 (Item 6 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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13263730 BIOSIS NO.: 200100470879

RTX toxin structure and function: A story of numerous anomalies and few analogies in toxin biology.

BOOK TITLE: Current Topics in Microbiology and Immunology Pore - forming toxins

AUTHOR: Welch R A(a)

BOOK AUTHOR/EDITOR: van der Goot F Gisou: Ed

AUTHOR ADDRESS: (a)Department of Medical Microbiology and Immunology, University of Wisconsin School of Medicine, Madison, WI, 53706\*\*USA

JOURNAL: Current Topics in Microbiology and Immunology 257p85-111 2001

MEDIUM: print

BOOK PUBLISHER: Springer-Verlag GmbH & Co. KG, Heidelberger Platz 3, D-14197, Berlin, Germany

Springer-Verlag New York Inc., 175 Fifth Avenue, New York, NY, 10010-7858, USA

ISSN: 0070-217X ISBN: 3-540-41386-3 (cloth)

DOCUMENT TYPE: Book

RECORD TYPE: Citation

LANGUAGE: English

SUMMARY LANGUAGE: English

REGISTRY NUMBERS: 14127-61-8: CALCIUM ION

DESCRIPTORS:

MAJOR CONCEPTS: Membranes (Cell Biology); Infection; Toxicology

ORGANISMS: PARTS ETC: membranes

**CHEMICALS & BIOCHEMICALS:** RTX toxin--function, structure; calcium ion; cell receptors; hemolysins--toxins

**MISCELLANEOUS TERMS:** apoptosis; necrosis; Book Chapter

**CONCEPT CODES:**

10069 Biochemical Studies-Minerals

10508 Biophysics-Membrane Phenomena

10802 Enzymes-General and Comparative Studies; Coenzymes

22501 Toxicology-General; Methods and Experimental

2/9/109 (Item 12 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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13133225 BIOSIS NO.: 200100340374

Analyses of the pore forming ability of *Bacillus thuringiensis* Cry1A mutant toxins using a light-scattering technique.

AUTHOR: Daniel Anu(a); Dean Donald H; Adang Michael J

AUTHOR ADDRESS: (a)Department of Biochemistry and Molecular Biology, University of Georgia, Athens, GA, 30602: adang@arches.uga.edu\*\*USA

JOURNAL: Pesticide Biochemistry and Physiology 70 (1):p7-18 May, 2001

MEDIUM: print

ISSN: 0048-3575

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

**ABSTRACT:** The pore formation properties of *Bacillus thuringiensis* Cry1 wild type and domain I and II mutant toxins were studied on *Manduca sexta* brush border membrane vesicles (BBMV) using a light-scattering technique. Wild type Cry1Ac, Cry1Ab, and Cry1Ba; Cry1Ab mutant toxins A92E, Y153D, R368A/R369A, and F371A; and Cry1Ac mutant toxin A92D were analyzed. In a direct mixing assay the mutant toxins Y153D, R368A/R369A, F371A, and Cry1Ba did not elicit a response in a 1-min signal-monitoring period.

Mutant toxins A92D and A92E elicited slight responses. After preincubation of toxin with BBMV, the signal recovery response increased for all toxins. The signal recoveries caused by A92D and A92E were greater than Y153D-, F371A-, and R368A/R369A-induced signal recoveries, which were slightly greater than Cry1Ba-induced recoveries. By increasing the monitoring period to 3 min in direct mixing experiments, we observed greater pore formation by A92D. A92E had a response similar to, but lower than that of A92D. The response induced by both wild type and mutant toxins decreased when the hyperosmotic solution was changed from KCl to sucrose. However, in the presence of sucrose the responses induced by

A 107

A92D and A92E were substantially reduced relative to KCl.

REGISTRY NUMBERS: 57-50-1: SUCROSE

DESCRIPTORS:

MAJOR CONCEPTS: Pesticides; Toxicology

BIOSYSTEMATIC NAMES: Endospore-forming Gram-Positives--Eubacteria, Bacteria, Microorganisms; Lepidoptera--Insecta, Arthropoda, Invertebrata, Animalia

ORGANISMS: *Bacillus thuringiensis* (Endospore-forming Gram-Positives); *Manduca sexta* (Lepidoptera)

ORGANISMS: PARTS ETC: brush border membrane vesicles {BBMV}

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Arthropods; Bacteria; Eubacteria; Insects; Invertebrates; Microorganisms

CHEMICALS & BIOCHEMICALS: Cry1A mutant toxins--bioinsecticide; sucrose

METHODS & EQUIPMENT: light-scattering technique--analytical method

MISCELLANEOUS TERMS: pore formation properties

CONCEPT CODES:

31000 Physiology and Biochemistry of Bacteria

10068 Biochemical Studies-Carbohydrates

22501 Toxicology-General; Methods and Experimental

54600 Pest Control, General; Pesticides; Herbicides

64076 Invertebrata, Comparative and Experimental Morphology, Physiology and Pathology-Insecta-Physiology

BIOSYSTEMATIC CODES:

07810 Endospore-forming Gram-Positives (1992- )

75330 Lepidoptera

2/9/122 (Item 25 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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12733510 BIOSIS NO.: 200000487012

Relationship of structure to function in the pore - forming toxin pneumolysin from *Streptococcus pneumoniae*.

AUTHOR: El-Rachkidy R(a); Davies N W; Andrew P W(a)

AUTHOR ADDRESS: (a)Department of Microbiology and Immunology, University of Leicester, Leicester, LE1 9HN\*\*UK

JOURNAL: Medical Microbiology and Immunology 189 (1):p35 September, 2000

MEDIUM: print

CONFERENCE/MEETING: 4th International Workshop on Pore-Forming Toxins

Trento, Italy September 14-17, 2000

ISSN: 0300-8584

RECORD TYPE: Citation

LANGUAGE: English

SUMMARY LANGUAGE: English

REGISTRY NUMBERS: 122-19-0: CATIONS

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Membranes (Cell Biology); Toxicology

BIOSYSTEMATIC NAMES: Animalia; Gram-Positive Cocci--Eubacteria, Bacteria, Microorganisms

ORGANISMS: *Streptococcus pneumoniae* (Gram-Positive Cocci)--pathogen; animal (Animalia)--host

ORGANISMS: PARTS ETC: cell membranes--analysis

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Bacteria; Eubacteria; Microorganisms

CHEMICALS & BIOCHEMICALS: bacterial toxins--action mechanisms, analysis, biological properties, molecular properties; cations; pneumolysin--action mechanisms, analysis, biological properties, molecular properties, pore-forming bacterial toxin; toxins--action mechanisms, analysis, biological properties, molecular properties

MISCELLANEOUS TERMS: electrophysiology; point mutations; structure-function relationships--analysis; Meeting Abstract

CONCEPT CODES:

10508 Biophysics-Membrane Phenomena

02506 Cytology and Cytochemistry-Animal

10060 Biochemical Studies-General

22501 Toxicology-General; Methods and Experimental

30500 Morphology and Cytology of Bacteria

31000 Physiology and Biochemistry of Bacteria

00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals

BIOSYSTEMATIC CODES:

07700 Gram-Positive Cocci (1992- )

33000 Animalia-Unspecified

2/9/127 (Item 30 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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12486973 BIOSIS NO.: 200000240475

Structure-activity study of equinatoxins, pore - forming toxins from sea anemone.

AUTHOR: Anderluh Gregor(a); Barlic Ariana(a); Podlesek Zdravko(a); Menestrina Gianfranco; Macek Peter(a)

AUTHOR ADDRESS: (a)Department of Biology, University of Ljubljana, Vecna Pot 111, 1000, Ljubljana\*\*Slovenia

JOURNAL: Pfluegers Archiv European Journal of Physiology 439 (3 Suppl.):p

R124 2000

CONFERENCE/MEETING: 1998 Life Sciences Conference: Signalling Concepts in Life Sciences. Godz Martuljek, Slovenia September 19-24, 1998

ISSN: 0031-6768

RECORD TYPE: Citation

LANGUAGE: English

SUMMARY LANGUAGE: English

REGISTRY NUMBERS: 52-90-4Q: CYSTEINE; 3374-22-9Q: CYSTEINE; 107852-47-1Q: EQUINATOXIN II; 146836-99-9Q: EQUINATOXIN II; 54-12-6Q: TRYPTOPHAN; 73-22-3Q: TRYPTOPHAN

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Toxicology

BIOSYSTEMATIC NAMES: Cnidaria--Invertebrata, Animalia; Enterobacteriaceae

--Facultatively Anaerobic Gram-Negative Rods, Eubacteria, Bacteria,

Microorganisms

ORGANISMS: Actinia equina { sea anemone} (Cnidaria); Escherichia coli (Enterobacteriaceae)

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Bacteria; Eubacteria; Invertebrates; Microorganisms

CHEMICALS & BIOCHEMICALS: arginine 144; biotin maleimide; cysteine; equinatoxin II--pore-forming toxin, toxin; hemolysin; serine 160; tryptophan

MISCELLANEOUS TERMS: Meeting Abstract

CONCEPT CODES:

10060 Biochemical Studies-General

13002 Metabolism-General Metabolism; Metabolic Pathways

22501 Toxicology-General; Methods and Experimental

00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals

BIOSYSTEMATIC CODES:

06702 Enterobacteriaceae (1992- )

41000 Cnidaria

2/9/126 (Item 29 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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12653331 BIOSIS NO.: 200000406833

Pore - forming toxins as cell-biological and pharmacological tools.

BOOK TITLE: Handbook of Experimental Pharmacology; Bacterial protein toxins

AUTHOR: Ahnert-Hilger G(a); Pahner I(a); Hoeltje M(a)

BOOK AUTHOR/EDITOR: Aktories Klaus; Just Ingo: Authors

AUTHOR ADDRESS: (a)Institut fuer Anatomie, Universitaetsklinikum Charite

der Humboldt-Universitaet zu Berlin, Philippstr. 12, D-10115, Berlin\*\*

Germany

JOURNAL: *Handbook of Experimental Pharmacology* 145p557-575 2000

MEDIUM: print

BOOK PUBLISHER: Springer Verlag, 175 Fifth Avenue, New York, NY, 10010, USA

Springer-Verlag, Heidelberger Platz 3, D-14197, Berlin,

Germany

ISSN: 0171-2004 ISBN: 3-540-66125-5 (cloth)

DOCUMENT TYPE: Book

RECORD TYPE: Citation

LANGUAGE: English

SUMMARY LANGUAGE: English

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Pharmacology; Toxicology

BIOSYSTEMATIC NAMES: Leporidae--Lagomorpha, Mammalia, Vertebrata, Chordata, Animalia; Micrococcaceae--Gram-Positive Cocci, Eubacteria, Bacteria, Microorganisms; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: PC12 cell line (Muridae)--rat pheochromocytoma cells; *Staphylococcus aureus* (Micrococcaceae); rabbit (Leporidae)

ORGANISMS: PARTS ETC: erythrocytes--blood and lymphatics

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Bacteria; Chordates; Eubacteria; Lagomorphs; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

CHEMICALS & BIOCHEMICALS: alpha-toxin--pore-forming toxin; pore-forming toxins--cell-biological tool, pharmacological tool; streptolysin O--pore-forming toxin

MISCELLANEOUS TERMS: Book Chapter

CONCEPT CODES:

02506 Cytology and Cytochemistry-Animal

10060 Biochemical Studies-General

12512 Pathology, General and Miscellaneous-Therapy (1971- )

15002 Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph Studies

15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies

22002 Pharmacology-General

22501 Toxicology-General; Methods and Experimental

31000 Physiology and Biochemistry of Bacteria

BIOSYSTEMATIC CODES:

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07702 Micrococcaceae (1992- )

86040 Leporidae

86375 Muridae

2/9/125 (Item 28 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2002 BIOSIS. All rts. reserv.

12733487 BIOSIS NO.: 200000486989  
4th International Workshop on Pore - Forming Toxins .  
AUTHOR: Anonymous  
JOURNAL: Medical Microbiology and Immunology 189 (1):p28-54 September, 2000  
MEDIUM: print  
CONFERENCE/MEETING: 4th International Workshop on Pore-Forming Toxins  
Trento, Italy September 14-17, 2000  
ISSN: 0300-8584  
RECORD TYPE: Citation  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
DESCRIPTORS:  
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Membranes (Cell Biology); Toxicology  
CHEMICALS & BIOCHEMICALS: toxins--action mechanisms, analysis, molecular structure  
MISCELLANEOUS TERMS: Abstracts only  
CONCEPT CODES:  
10508 Biophysics-Membrane Phenomena  
10060 Biochemical Studies-General  
22501 Toxicology-General; Methods and Experimental  
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals

2/9/128 (Item 31 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2002 BIOSIS. All rts. reserv.

12464694 BIOSIS NO.: 200000218196  
Mechanism of membrane translocation by anthrax toxin : Insertion and pore formation by protective antigen.  
AUTHOR: Collier R J(a)  
AUTHOR ADDRESS: (a)Microbiology and Molecular Genetics, Harvard Medical School, 200 Longwood Avenue, Boston, MA, 02115\*\*USA  
JOURNAL: Journal of Applied Microbiology 87(2):p283-Aug., 1999  
CONFERENCE/MEETING: 3rd International Conference on Anthrax Plymouth, England, UK September 7-10, 1998  
ISSN: 1364-5072  
RECORD TYPE: Citation

LANGUAGE: English

SUMMARY LANGUAGE: English

DESCRIPTORS:

MAJOR CONCEPTS: Infection

BIOSYSTEMATIC NAMES: Animalia; Endospore-forming Gram-Positives--  
Eubacteria, Bacteria, Microorganisms

ORGANISMS: *Bacillus anthracis* (Endospore-forming Gram-Positives)--  
pathogen; animal (Animalia)

ORGANISMS: PARTS ETC: cell membranes

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Bacteria; Eubacteria;  
Microorganisms

DISEASES: anthrax--bacterial disease

CHEMICALS & BIOCHEMICALS: anthrax toxin--membrane translocation  
mechanisms; bacterial antigens; edema factor; lethal factor;  
protective antigen

MISCELLANEOUS TERMS: Meeting Abstract

ALTERNATE INDEXING: Anthrax (MeSH)

CONCEPT CODES:

36002 Medical and Clinical Microbiology-Bacteriology

02502 Cytology and Cytochemistry-General

10064 Biochemical Studies-Proteins, Peptides and Amino Acids

10506 Biophysics-Molecular Properties and Macromolecules

12502 Pathology, General and Miscellaneous-General

31000 Physiology and Biochemistry of Bacteria

34504 Immunology and Immunochemistry-Bacterial, Viral and Fungal

22501 Toxicology-General; Methods and Experimental

10508 Biophysics-Membrane Phenomena

00520 General Biology-Symposia, Transactions and Proceedings of  
Conferences, Congresses, Review Annuals

BIOSYSTEMATIC CODES:

07810 Endospore-forming Gram-Positives (1992- )

33000 Animalia-Unspecified

?t s2/9/134 141 147 151 157 160 185 186 190 191 204 206

2/9/134 (Item 37 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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11678744 BIOSIS NO.: 199800460475

Lys-77 is important for hemolytic activity of equinatoxin II, a pore  
forming toxin from the sea anemone *Actinia equina*.

AUTHOR: Anderluh G(a); Barlic A(a); Pungercar J; Menestrina G; Gubensek F;  
Macek P(a)

AUTHOR ADDRESS: (a)Dep. Biol., Biotechnical Fac., Univ. Ljubljana, Vecna  
pot 111, Ljubljana\*\*Slovenia

JOURNAL: *Toxicon* 36 (9):p1270 Sept., 1998

CONFERENCE/MEETING: 12th World Congress on Animal, Plant and Microbial Toxins Cuernavaca, Mexico, USA September 21-26, 1997

ISSN: 0041-0101

RECORD TYPE: Citation

LANGUAGE: English

REGISTRY NUMBERS: 107852-47-1Q: EQUINATOXIN II; 146836-99-9Q: EQUINATOXIN II

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Toxicology

BIOSYSTEMATIC NAMES: Cnidaria--Invertebrata, Animalia

ORGANISMS: *Actinia-equina* {sea anemone} (Cnidaria)

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Invertebrates

CHEMICALS & BIOCHEMICALS: equinatoxin II--hemolytic activity, pore forming toxin; lysine-77

MISCELLANEOUS TERMS: Meeting Abstract; Meeting Poster

CONCEPT CODES:

22501 Toxicology-General; Methods and Experimental

10060 Biochemical Studies-General

15001 Blood, Blood-Forming Organs and Body Fluids-General; Methods

00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals

BIOSYSTEMATIC CODES:

41000 Cnidaria

2/9/141 (Item 44 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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10820895 BIOSIS NO.: 199799442040

Pore formation by diphtheria toxin is dependent on protein concentration.

AUTHOR: Sharpe J C; London E

AUTHOR ADDRESS: Dep. Biochemistry Cell Biol., SUNY Stony Brook, Stony Brook, NY 11794-5215\*\*USA

JOURNAL: *Biophysical Journal* 72 (2 PART 2):pA310 1997

CONFERENCE/MEETING: 41st Annual Meeting of the Biophysical Society New Orleans, Louisiana, USA March 2-6, 1997

ISSN: 0006-3495

RECORD TYPE: Citation

LANGUAGE: English

REGISTRY NUMBERS: 58517-16-1: DIPHTHERIA TOXIN; 9004-54-0: DEXTRAN

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Membranes (Cell

Biology); Toxicology  
CHEMICALS & BIOCHEMICALS: DIPHTHERIA TOXIN; DEXTRAN  
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Poster; BIOCHEMISTRY AND BIOPHYSICS; DEXTRAN; DIPHTHERIA TOXIN; LIPID-PROTEIN INTERACTION; MEMBRANE LIPID COMPOSITION; MEMBRANES; MOLECULAR SIZE; PORE FORMATION

CONCEPT CODES:

- 10064 Biochemical Studies-Proteins, Peptides and Amino Acids
- 10066 Biochemical Studies-Lipids
- 10506 Biophysics-Molecular Properties and Macromolecules
- 10508 Biophysics-Membrane Phenomena
- 22501 Toxicology-General; Methods and Experimental
- 00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals

2/9/147 (Item 50 from file: 5)  
DIALOG(R)File 5.Biosis Previews(R)  
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10078829 BIOSIS NO.: 199598533747  
Pore - forming toxins of gram-positive bacteria.  
BOOK TITLE: Virulence mechanisms of bacterial pathogens, Second edition  
AUTHOR: Tweten Rodney K  
BOOK AUTHOR/EDITOR: Roth J A; Bolin C A; Brogden K A; Minion F C; Wannemuehler M J: Eds  
AUTHOR ADDRESS: Dep. Microbiol. Immunol., Univ. Okla. Health Sci. Center, Oklahoma City, OK 73190\*\*USA  
p207-229 1995  
BOOK PUBLISHER: American Society for Microbiology (ASM), Books Division, 1325 Massachusetts Ave. NW, Washington, DC 20005-4171, USA

CONFERENCE/MEETING: International Symposium Ames, Iowa, USA June 6-8, 1994

ISBN: 1-55581-085-3

RECORD TYPE: Citation

LANGUAGE: English

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Genetics; Infection; Physiology

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BIOSYSTEMATIC NAMES: Animalia=Unspecified--Animalia; Endospore-forming Gram-Positives--Eubacteria, Bacteria; Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Micrococcaceae--Eubacteria, Bacteria; Regular Nonsporing Gram-Positive Rods--Eubacteria, Bacteria; Vertebrata-Unspecified--Vertebrata, Chordata, Animalia

ORGANISMS: animal (Animalia - Unspecified); endospore-forming gram-positive rods and cocci (Endospore-forming Gram-Positives); human (Hominidae); regular nonsporing gram-positive rods (Regular Nonsporing Gram-Positive Rods); Animalia (Animalia - Unspecified); Clostridium septicum (Endospore-forming Gram-Positives); Listeria monocytogenes (Regular Nonsporing Gram-Positive Rods); Staphylococcus aureus (Micrococcaceae); Vertebrata (Vertebrata - Unspecified)

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; bacteria; chordates; eubacteria; humans; mammals; microorganisms; nonhuman vertebrates; primates; vertebrates

MISCELLANEOUS TERMS: BACTERIAL VIRULENCE; BOOK CHAPTER; CYTOLYTIC

MECHANISM; ETIOLOGY; EUKARYOTIC CELLS; MEETING PAPER; OLIGOMERIZATION; PATHOGENESIS

CONCEPT CODES:

10062 Biochemical Studies-Nucleic Acids, Purines and Pyrimidines

10064 Biochemical Studies-Proteins, Peptides and Amino Acids

31000 Physiology and Biochemistry of Bacteria

31500 Genetics of Bacteria and Viruses

36002 Medical and Clinical Microbiology-Bacteriology

00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals

10052 Biochemical Methods-Nucleic Acids, Purines and Pyrimidines

BIOSYSTEMATIC CODES:

07702 Micrococcaceae (1992- )

07810 Endospore-forming Gram-Positives (1992- )

07830 Regular Nonsporing Gram-Positive Rods (1992- )

33000 Animalia-Unspecified

85150 Vertebrata-Unspecified

86215 Hominidae

2/9/151 (Item 54 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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09330333 BIOSIS NO.: 199497338703

Pore formation by *E. coli* hemolysin and related RTX toxins in model membranes and target cells.

BOOK-TITLE: FEMS-Symposium; Bacterial-protein-toxins

AUTHOR: Menestrina G(a); Dalla Serra M(a); Pederzolli C(a); Moser C(a); Pellet S; Welch R; Gambale F

BOOK AUTHOR/EDITOR: Freer J; Aitken R; Alouf J E; Boulnois G: Eds

AUTHOR ADDRESS: (a)CENTRO CNR-ITC Fisica Stati Aggregati, Via Sommarive 14,

I-38050 Povo\*\*Italy

JOURNAL: FEMS Symposium (73):p312-321 1994

BOOK PUBLISHER: Gustav Fischer Verlag, Wollgrasweg 49, D-7000 Stuttgart, Germany

Gustav Fischer Verlag, New York, New York, USA

CONFERENCE/MEETING: Sixth European Workshop Stirling, Scotland, UK June 27-July 2, 1993

ISSN: 0163-9188 ISBN: 3-437-11535-9; 1-56081-385-7

RECORD TYPE: Citation

LANGUAGE: English

REGISTRY NUMBERS: 113972-57-9: LEUKOTOXIN

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Hematology (Human Medicine, Medical Sciences); Infection; Physiology; Toxicology

BIOSYSTEMATIC NAMES: Alcaligenaceae--Eubacteria, Bacteria; Enterobacteriaceae--Eubacteria, Bacteria; Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Pasteurellaceae--Eubacteria, Bacteria

ORGANISMS: human (Hominidae); Actinobacillus (Pasteurellaceae); Bordetella (Alcaligenaceae); Escherichia coli (Enterobacteriaceae); Morganella (Enterobacteriaceae); Pasteurella (Pasteurellaceae); Proteus (Enterobacteriaceae)

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; bacteria; chordates; eubacteria; humans; mammals; microorganisms; primates; vertebrates

CHEMICALS & BIOCHEMICALS: LEUKOTOXIN

MISCELLANEOUS TERMS: BOOK CHAPTER; CYTOTOXIC MECHANISM;

ERYTHROCYTE

HOST; LEUKOTOXIN; MACROPHAGE; MEETING PAPER; VIRULENCE FACTOR

CONCEPT CODES:

02506 Cytology and Cytochemistry-Animal

10506 Biophysics-Molecular Properties and Macromolecules

15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies

15006 Blood, Blood-Forming Organs and Body Fluids-Blood, Lymphatic and Reticuloendothelial Pathologies

15008 Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and Reticuloendothelial System

22501 Toxicology-General; Methods and Experimental

31000 Physiology and Biochemistry of Bacteria

36002 Medical and Clinical Microbiology-Bacteriology

00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review-Annuals

02508 Cytology and Cytochemistry-Human

BIOSYSTEMATIC CODES:

06502 Alcaligenaceae (1992- )

06702 Enterobacteriaceae (1992- )

06703 Pasteurellaceae (1992- )

86215 Hominidae

2/9/157 (Item 60 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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08706345 BIOSIS NO.: 199345124420

Second International Workshop on Pore - Forming Toxins , Mainz, Germany,  
September 29-October 2, 1993.

AUTHOR: Bhakdi S(a); Fleischer B; Rott R

AUTHOR ADDRESS: (a)Inst. Med. Mikrobiol., Univ. Obere Zahlbacher Str. 67,  
Hochhaus am Augustusplatz, D-55101 Mainz\*\*Germany

JOURNAL: Medical Microbiology and Immunology 182 (4):p177-221 1993

CONFERENCE/MEETING: Second International Workshop on Pore-Forming Toxins  
Mainz, Germany September 29-October 2, 1993

ISSN: 0300-8584

RECORD TYPE: Citation

LANGUAGE: English

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Membranes (Cell  
Biology); Physiology; Toxicology

BIOSYSTEMATIC NAMES: Bacteria-General Unspecified--Eubacteria, Bacteria;  
Fungi-Unspecified--Fungi, Plantae

ORGANISMS: bacteria (Bacteria - General Unspecified); fungi (Fungi -  
Unspecified)

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): bacteria; eubacteria; fungi;  
microorganisms; nonvascular plants; plants

MISCELLANEOUS TERMS: ABSTRACTS ONLY; PROTEIN

CONCEPT CODES:

10064 Biochemical Studies-Proteins, Peptides and Amino Acids

10506 Biophysics-Molecular Properties and Macromolecules

10508 Biophysics-Membrane Phenomena

22501 Toxicology-General; Methods and Experimental

31000 Physiology and Biochemistry of Bacteria

51522 Plant Physiology, Biochemistry and Biophysics-Chemical  
Constituents

00520 General Biology-Symposia, Transactions and Proceedings of  
Conferences, Congresses, Review Annuals

---

BIOSYSTEMATIC CODES:

05000 Bacteria-General Unspecified (1992- )

15000 Fungi-Unspecified

2/9/185 (Item 6 from file: 143)  
DIALOG(R)File 143:Biol. & Agric. Index  
(c) 2002 The HW Wilson Co. All rts. reserv.

0432120 H.W. WILSON RECORD NUMBER: BBAI93031009  
Altered pore - forming properties of proteolytically nicked  
staphylococcal a- toxin  
Palmer, Michael  
Weller, Ulrich; Messner, Martina  
The Journal of Biological Chemistry v. 268 (June 5 '93) p. 11963-7  
DOCUMENT TYPE: Feature Article ISSN: 0021-9258 LANGUAGE: English  
RECORD STATUS: New record

DESCRIPTORS: Staphylococcus toxins; Proteolysis

2/9/186 (Item 1 from file: 65)  
DIALOG(R)File 65:Inside Conferences  
(c) 2002 BLDSC all rts. reserv. All rts. reserv.

03791205 INSIDE CONFERENCE ITEM ID: CN039842324  
Insights into Ion Channels: Structural Studies of Pore - forming Protein  
Toxins  
Parker, M. W.  
CONFERENCE: Protein structure and function-Annual conference; 26th  
ANNUAL LORNE CONFERENCE ON PROTEIN STRUCTURE AND FUNCTION, 2001;  
26TH  
P: O6  
Lorne, 2001  
ISSN: 1034-3180  
LANGUAGE: English DOCUMENT TYPE: Conference Selected short papers & abstracts  
CONFERENCE LOCATION: Lorne, Australia 2001; Feb (200102) (200102)

BRITISH LIBRARY ITEM LOCATION: 1087.311620  
NOTE:

Also known as the 26th Lorne protein conference, 2001  
DESCRIPTORS: protein structure

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2/9/190 (Item 5 from file: 65)  
DIALOG(R)File 65:Inside Conferences  
(c) 2002 BLDSC all rts. reserv. All rts. reserv.

03437034 INSIDE CONFERENCE ITEM ID: CN036265425

Aerolysin -Studies of a Pore - Forming Toxin  
Feil, S. C.; Rossjohn, J.; McKinstry, W. J.; Buckley, J. T.; Parker, M. W.  
CONFERENCE: Protein structure and function-Annual conference; 25th ANNUAL LORNE CONFERENCE ON PROTEIN STRUCTURE AND FUNCTION, 2000; 25TH  
P: A85  
Lorne, 2000  
ISSN: 1034-3180  
LANGUAGE: English DOCUMENT TYPE: Conference Selected short papers, abstracts and programme  
CONFERENCE LOCATION: Lorne, Australia  
CONFERENCE DATE: Feb 2000  
BRITISH LIBRARY ITEM LOCATION: 1087.311620  
NOTE:  
Also known as the 25th Lorne protein conference, 2000  
DESCRIPTORS: protein structure

2/9/191 (Item 6 from file: 65)  
DIALOG(R)File 65:Inside Conferences  
(c) 2002 BLDSC all rts. reserv. All rts. reserv.  
02712893 INSIDE CONFERENCE ITEM ID: CN028243503  
Pore - forming toxins with built-in triggers and switches  
Bayley, H.  
CONFERENCE: Toxins-Joint interest group symposium  
SOCIETY FOR APPLIED MICROBIOLOGY SYMPOSIUM SERIES, 1998; NUMB 27 P: 151S  
Blackwell Science, 1998  
ISSN: 0267-4440  
LANGUAGE: English DOCUMENT TYPE: Conference Papers  
CONFERENCE EDITOR(S): Mitchell, T. J.; Godfree, A. F.; Stewart-Tull, D. E. S.  
CONFERENCE SPONSOR: Society for Applied Microbiology  
CONFERENCE LOCATION: Norwich 1997 (199700) (199700)  
BRITISH LIBRARY ITEM LOCATION: 8319.193420  
DESCRIPTORS: toxins; SfAM; applied microbiology; microbiology

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2/9/204 (Item 2 from file: 35)  
DIALOG(R)File 35:Dissertation Abs Online  
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01663951 ORDER NO: AAD99-04251

DIPHTHERIA TOXIN PORE FORMATION AND OLIGOMERIZATION IN  
MEMBRANES:

IMPLICATIONS FOR CATALYTIC DOMAIN TRANSLOCATION

Author: SHARPE, JUANITA CARLA

Degree: PH.D.

Year: 1998

Corporate Source/Institution: STATE UNIVERSITY OF NEW YORK AT STONY  
BROOK (0771)

Adviser: ERWIN LONDON

Source: VOLUME 59/08-B OF DISSERTATION ABSTRACTS INTERNATIONAL.  
PAGE 4094. 221 PAGES

Descriptors: CHEMISTRY, BIOCHEMISTRY ; BIOPHYSICS, GENERAL ; BIOLOGY,  
CELL

Descriptor Codes: 0487; 0786; 0379

Diphtheria toxin is a cytotoxic protein which has the ability to enter and kill cells by the transfer of its catalytic fragment across cellular endosomes. The mechanism of the translocation of the catalytic fragment is unknown, but it has been suggested that the translocation could occur through a pore. The pores formed by diphtheria toxin have been reported to be as small as 5 Å in diameter and as large as to translocate, nor the involvement of the pore in the translocation of the catalytic domain across bilayers. An assay was developed called the dextran leakage assay. This assay involves the trapping of fluorescently labeled dextrans of various sizes inside the lumen of large unilamellar vesicles. The ability of these fluorescently labeled dextrans to escape was detected through the use of antibodies directed against the fluorescent probe attached to the dextran which have the ability to bind to the probe and quench its fluorescence. Using this technique it was found that diphtheria toxin forms concentration dependent pores, that is, at low concentrations toxin pores are small and as the concentration of the toxin in the membrane increases the pore size increases. Toxin oligomerization was found to occur in the membrane and using a combination of chemical crosslinking and rhodamine-self quenching, it was found that the toxin formed non-stoichiometric oligomers. The size of the pores formed by the toxin were affected by addition of cholesterol which increased either the pore number or pore size. In investigating the contribution of the transmembrane domain (T domain) to diphtheria toxin pore formation it was found that the T domain formed concentration dependent pores similar to those of whole toxin but were larger at higher protein concentrations. It was proposed that since the T domain forms larger pores than whole toxin that the catalytic and receptor binding domains of the toxin contributed to the structure of the pore. From these data a mechanism of catalytic domain translocation was proposed in which pore formation was the result of the oligomerization of the toxin in the

membrane. The oligomerization may promote the correct membrane orientation of the toxin such that the catalytic domain is correctly positioned for translocation. It was also found that a class of cyclic compounds could inhibit pore formation by diphtheria toxin. Though each of these compounds could inhibit pore formation through steric binding to the channel, inhibition could also occur through several other mechanisms. Continuing studies of the use of these compounds may prove useful in the analysis of other membrane active and pore forming proteins.

2/9/206 (Item 4 from file: 35)  
DIALOG(R)File 35:Dissertation Abs Online  
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01465373 ORDER NO: AADAA-IMM00880  
TOXIN -MEMBRANE BINDING AND PORE FORMATION IN THE TRANSLOCATION  
MECHANISM OF EXOTOXIN A'S CYTOTOXIC ACTIVITY

Author: RASPER, DITA M.

Degree: M.SC.

Year: 1995

Corporate Source/Institution: UNIVERSITY OF GUELPH (CANADA) (0081)

Adviser: A. R. MERRILL

Source: VOLUME 34/02 of MASTERS ABSTRACTS.

PAGE 760. 128 PAGES

Descriptors: CHEMISTRY, BIOCHEMISTRY ; BIOLOGY, CELL

Descriptor Codes: 0487; 0379

ISBN: 0-315-00880-0

Binding of *Pseudomonas* Exotoxin A (ETA) to model endosomal membrane vesicles was evaluated by a fluorescence quenching technique. The binding of toxin to various large, unilamellar vesicles composed of POPC and POPS was highly pH-dependent (maximal binding at pH 4.0,  $K_m$  = 2  $\mu M$ ; 60:40 (mol:mol), POPC/POPS), however, was NaCl concentration-independent. The rate of toxin-induced pore formation in the lipid bilayer was pH-dependent (increasing with decreasing pH), with optimal dye release occurring at pH 4.0 ( $pK_m$  = 4.3-\$4.5). Pore formation was also sensitive to the NaCl concentration of the assay buffer, with maximal release occurring at 50 mM NaCl (decreasing with increasing salt concentration), indicating that the toxin-induced pore is modulated by ionic interactions. Further evidence for the role of electrostatic interactions between ETA and the membrane was provided by the effect of POPS on the kinetic properties of the pore. The magnitude of dye release (at 50 mM NaCl) according to mole % POPS content was as follows; 100 mole % < 20 mole % < 60 mole %, indicating the requirement of an optimum negative surface charge density. Pore formation was temperature-dependant,  $E_m$  = 13.3

kcal/mole, and sensitive to the physical state of the bilayer.

?logoff hold